

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF :
Claudio CAVAZZA : NEW APPLICATIONS BRANCH
SERIAL NO.: NEW APPLICATION :
FILED: HEREWITH :
FOR: PHARMACEUTICAL COMPOSITION :
COMPRISING CARNITINE OR
ALKANOYL L-CARNITINE, FOR THE
PREVENTION AND TREATMENT OF
DISEASES BROUGHT ABOUT BY
LIPID METABOLISM DISORDERS

PRELIMINARY AMENDMENT

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

SIR:

Prior to examination on the merits, the Applicants respectfully request entry of the following amendments.

IN THE SPECIFICATION

On page 2 of the specification, substitute the paragraph below for the paragraph on original lines 10 through 17.

--Hydroxycitric acid and derivatives thereof may occur as extracts of natural products containing hydroxycitric acid at high concentrations, such as the extract of the fruits of Garcinia (Garcinia cambogia, Garcinia atroviridis, Garcinia indica, Garcinia citrin), of the fruits of Malabar Tamarind or Gorikapuli (Lewis Y. L., Neelakantan S., Phyto-chemistry 4, 619, 1965), (Streenivasan A., Vankataraman R., Current Science 4, 151, 1959) or other extract of natural products containing same.--

On page 13 of the specification, substitute the number 7 entry below for the number 7 entry on original lines 22 through 23.

--7) L-carnitinemg 500

Garcinia cambogia extract mg 500--.

On page 14 of the specification, substitute the numbers 8, 9, 10, 11 and 12 entries below for the numbers 8, 9, 10, 11 and 12 entries on original lines 2 through 15.

--8) Acetyl L-carnitinemg 500

Garcinia cambogia extract mg 500

(30% hydroxycitric acid)

9) Propionyl L-carnitinemg 500

Garcinia cambogia extract mg 500

(30% hydroxycitric acid)

10) Isovaleryl L-carnitinemg 500

Garcinia cambogia extract mg 500

(30% hydroxycitric acid)

11) Valeryl L-carnitinemg 500

Garcinia cambogia extract mg 500

(30% hydroxycitric acid)

12) Butyryl L-carnitinemg 500

Garcinia cambogia extract mg 500--.

Replace all the text (paragraphs) on pages 16-20, with the text (paragraphs) on substitute pages 16-20 attached below:

TABLE I
MEAN DAILY FOOD CONSUMPTION (g) PER ANIMAL

	Before treatment	After 15 days
Calcium hydroxycitrate (g 1/100 g diet)	19.2 ± 0.65	17.1 ± 0.35
Calcium hydroxycitrate (g 2/100 g diet)	18.8 ± 0.44	15.1 ± 0.46
L-carnitine (g 2/100 g diet)	17.3 ± 0.35	18.1 ± 0.50
L-carnitine (g 4/100 g diet)	18.4 ± 0.61	17.8 ± 0.41
Acetyl L-carnitine (g 2/100 g diet)	18.6 ± 0.39	18.4 ± 0.44
Acetyl L-carnitine (g 4/100 g diet)	18.2 ± 0.41	18.8 ± 0.57
Propionyl L-carnitine (g 2/100 g diet)	17.7 ± 0.56	17.1 ± 0.38
Propionyl L-carnitine (g 4/100 g diet)	18.2 ± 0.44	18.5 ± 0.48
Garcinia cambogia (g 4/100 g diet)	17.9 ± 0.34	16.8 ± 0.44
Calcium hydroxycitrate (g 1/100 g diet) + L-carnitine (g 2/100 g diet)	18.9 ± 0.61	14.4 ± 0.50
Calcium hydroxycitrate (g 1/100 g diet) + Acetyl L-carnitine (g 2/100 g diet)	19.1 ± 0.58	14.8 ± 0.64
Calcium hydroxycitrate (g 1/100 g diet) + Propionyl L-carnitine (g 2/100 g diet)	18.4 ± 0.49	13.2 ± 0.53
L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet)	18.1 ± 4.7	15.9 ± 4.1
Acetyl L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet)	18.8 ± 3.9	16.2 ± 4.9
Propionyl L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet)	18.1 ± 4.8	14.4 ± 4.7

TABLE 2**BODY WEIGHT INCREASE AFTER 15 DAY-TREATMENT**

	Final body weight increase (g)
Controls	62.8 ± 3.5
Calcium hydroxycitrate (g 1/100 g diet)	46.6 ± 4.1
Calcium hydroxycitrate (g 2/100 g diet)	38.9 ± 3.8
L-carnitine (g 2/100 g diet)	66.2 ± 4.9
L-carnitine (g 4/100 g diet)	64.5 ± 5.1
Acetyl L-carnitine (g 2/100 g diet)	60.4 ± 7.1
Acetyl L-carnitine (g 4/100 g diet)	60.1 ± 6.1
Propionyl L-carnitine (g 2/100 g diet)	62.4 ± 3.9
Propionyl L-carnitine (g 4/100 g diet)	58.7 ± 3.7
Garcinia cambogia (g 4/100 g diet)	51.4 ± 3.3
Calcium hydroxycitrate (g 1/100 g diet) + L-carnitine (g 2/100 g diet)	28.7 ± 4.4
Calcium hydroxycitrate (g 1/100 g diet) + Acetyl L-carnitine (g 2/100 g diet)	31.6 ± 3.9
Calcium hydroxycitrate (g 1/100 g diet) + Propionyl L-carnitine (g 2/100 g diet)	24.4 ± 2.8
L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet)	38.6 ± 3.1
Acetyl L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet)	36.8 ± 4.4
Propionyl L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet)	34.8 ± 6.5

TABLE 3**SERUM TRIGLYCERIDES AND EPIDIDIMAL FAT AFTER 15 DAY-TREATMENT**

	Triglycerides (mg/100 ml)	Epididimal fat (g)
Controls	94.68 ± 6.6	4.65 ± 0.41
Calcium hydroxycitrate (g 1/100 g diet)	76.84 ± 6.9	3.91 ± 0.36
Calcium hydroxycitrate (g 2/100 g diet)	73.66 ± 7.1	3.32 ± 0.9
L-carnitine (g 2/100 g diet)	92.55 ± 7.7	4.21 ± 4.1
L-carnitine (g 4/100 g diet)	90.44 ± 6.8	4.34 ± 2.9
Acetyl L-carnitine (g 2/100 g diet)	95.81 ± 8.2	4.10 ± 3.8
Acetyl L-carnitine (g 4/100 g diet)	90.8 ± 7.5	4.15 ± 3.5
Propionyl L-carnitine (g 2/100 g diet)	88.4 ± 8.16	4.19 ± 4.4
Propionyl L-carnitine (g 4/100 g diet)	82.7 ± 6.6	4.0 ± 5.6
Garcinia cambogia (g 4/100 g diet)	80.4 ± 7.3	3.85 ± 3.5
Calcium hydroxycitrate (g 1/100 g diet) + L-carnitine (g 2/100 g diet)	71.5 ± 6.7	3.25 ± 2.9
Calcium hydroxycitrate (g 1/100 g diet) + Acetyl L-carnitine (g 2/100 g diet)	68.2 ± 5.5	3.0 ± 2.7
Calcium hydroxycitrate (g 1/100 g diet) + Propionyl L-carnitine (g 2/100 g diet)	60.5 ± 7.4	2.25 ± 2.2
L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet)	75.4 ± 3.1	3.50 ± 3.1
Acetyl L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet)	72.3 ± 4.4	3.25 ± 4.3
Propionyl L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet)	70.3 ± 5.6	2.95 ± 3.8

TABLE 4

TEST ON EXPERIMENTALLY-INDUCED HYPERTRIGLYCERIDAEMIA
(mg/100 ml)

Controls	195.8 ± 9.8
Calcium hydroxycitrate (g 0.5/Kg)	170.6 ± 8.5
Calcium hydroxycitrate (g 1/Kg)	145.5 ± 8.5
L-carnitine (g 0.5/Kg)	190.4 ± 9.6
L-carnitine (g 1/Kg)	190.8 ± 8.6
Acetyl L-carnitine (g 0.5/Kg)	191.2 ± 9.1
Acetyl L-carnitine (g 1/Kg)	188.4 ± 5.5
Propionyl L-carnitine (g 0.5/Kg)	184.2 ± 6.8
Propionyl L-carnitine (g 1/Kg)	180.4 ± 7.9
Garcinia cambogia (g 0.5/Kg)	170.6 ± 5.4
Calcium hydroxycitrate (g 0.5/Kg) + L-carnitine (g 0.5/Kg)	125.8 ± 9.1
Calcium hydroxycitrate (g 0.5/Kg) + Acetyl L-carnitine (g 0.5/Kg)	120.4 ± 8.8
Calcium hydroxycitrate (g 0.5/Kg) + Propionyl L-carnitine (g 0.5/Kg)	108 ± 9.4
L-carnitine (g 0.5/Kg) + Garcinia cambogia (g 0.5/Kg)	145.4 ± 8.6
Acetyl L-carnitine (g 0.5/Kg) + Garcinia cambogia (g 0.5/Kg)	140.4 ± 7.4
Propionyl L-carnitine (g 0.5/Kg) + Garcinia cambogia (g 0.5/Kg)	125 ± 8.5

TABLE 5
**TESTS ON EXPERIMENTALLY-INDUCED HYPERCHOLESTEROLEMIA
(TOTAL CHOLESTEROL mg/dl)**

Controls	92.5 ± 4.4
Hypercholesterolemic controls	270.5 ± 10.4
Calcium hydroxycitrate (g 1/100 g diet)	196.6 ± 9.6
Calcium hydroxycitrate (g 2/100 g diet)	180.5 ± 8.1
L-carnitine (g 2/100 g diet)	270.4 ± 5.1
L-carnitine (g 4/100 g diet)	260.6 ± 4.4
Acetyl L-carnitine (g 2/100 g diet)	266.7 ± 7.7
Acetyl L-carnitine (g 4/100 g diet)	255.4 ± 9.4
Propionyl L-carnitine (g 2/100 g diet)	250.6 ± 10.1
Propionyl L-carnitine (g 4/100 g diet)	235.3 ± 9.6
Garcinia cambogia (g 4/100 g diet)	250.7 ± 4.7
Calcium hydroxycitrate (g 1/100 g diet) + L-carnitine (g 2/100 g diet)	155.8 ± 8.8
Calcium hydroxycitrate (g 1/100 g diet) + Acetyl L-carnitine (g 2/100 g diet)	150.5 ± 7.1
Calcium hydroxycitrate (g 1/100 g diet) + Propionyl L-carnitine (g 2/100 g diet)	110.6 ± 6.6
L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet)	179.6 ± 9.6
Acetyl L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet)	165.9 ± 8.9
Propionyl L-carnitine (g 2/100 g diet) + Garcinia cambogia (g 4/100 g diet)	155.5 ± 6.8

IN THE CLAIMS

Cancel Claims 1-10.

Add new Claims 11-30

--11. A composition comprising:

- (i) a first component selected from the group consisting of C₂-C₈-alkanoyl L-carnitine and salts of C₂-C₈-alkanoyl L-carnitine; and
- (ii) a second component selected from the group consisting of a hydroxycitric acid, a hydroxycitric acid derivative, pantothenic acid, and a pantothenic acid derivative.

12. The composition of Claim 11, wherein the alkanoyl group of the first component is selected from the group consisting of acetyl, propionyl, butyryl, valeryl and isovaleryl.

13. The composition of Claim 11, wherein the first component is acetyl-L-carnitine, or a salt or ester thereof.

14. The composition of Claim 11, wherein the first component is propionyl-L-carnitine, or a salt or ester thereof.

15. The composition of Claim 14, wherein said pharmaceutically acceptable salt of propionyl L-carnitine is selected from the group consisting of propionyl L-carnitine chloride, propionyl L-carnitine bromide, propionyl L-carnitine orotate, propionyl L-carnitine acid aspartate, propionyl L-carnitine acid phosphate, propionyl L-carnitine fumarate, propionyl L-carnitine lactate, propionyl L-carnitine maleate, propionyl L-carnitine acid maleate, propionyl L-carnitine acid oxalate, propionyl L-carnitine acid sulfate, propionyl L-carnitine glucose phosphate, propionyl L-carnitine tartrate, and propionyl L-carnitine acid tartrate.

16. The composition of Claim 11, wherein the second component is selected from the group consisting of hydroxycitric acid, a salt of hydroxycitric acid, an ester of hydroxycitric acid, and a natural product or extract containing hydroxycitric acid or a salt or ester thereof.

17. The composition of Claim 11, wherein the second component is calcium

hydroxycitrate.

18. The composition of Claim 16, wherein said extract from the fruit selected from the group consisting of Garcinia, Malabar Tamarind and gorikapuli.
19. The composition of Claim 11, wherein the second component is selected from the group consisting of panthothenic acid, 4'-phosphopantethenate, 4'-phosphopantethenylcisteine, 4'-phosphopantotheine, pantotheine and pantethine.

20. The composition of Claim 11, wherein the weight ratio of the second component to the first component is:

1:1 to 1:100, when the second component is hydroxycitric acid or a derivative thereof,

and

10:1 to 1:100, when the second component is pantothenic acid or a derivative thereof.

21. The composition of Claim 11, further comprising a vitamin, mineral salt, antioxidant or vegetal fiber.

22. The composition of Claim 11, wherein said composition further comprises chromium.

23. The composition of Claim 11 in a solid, semisolid, liquid, semiliquid, powder, granular or lipsomic form.

24. The composition of Claim 11 in the form of a tablet, capsule, granulate, powder, or as contained within a vial suitable for oral, parenteral, rectal or topical administration.

25. A method for facilitating the metabolism of lipids, comprising administering to a subject in need thereof, an effective amount of the composition of Claim 11.

26. A method for reducing food consumption comprising administering to a subject in need thereof, an effective amount of the composition of Claim 11.

27. A method for reducing body weight comprising administering to a subject in need thereof, an effective amount of the composition of Claim 11.

28. A method for reducing serum triglycerides comprising administering to a subject in need thereof, an effective amount of the composition of Claim 11.

29. A method for treating hypertriglyceridaemia comprising administering to a subject in need thereof, an effective amount of the composition of Claim 11.

30. A method for treating hypercholesterolaemia comprising administering to a subject in need thereof, an effective amount of the composition of Claim 11.--

REMARKS

Claims 11-30 are pending. The specification has been amended to correct minor typographical errors, e.g. the word “*Garcinia cambodia*” has been corrected to “*Garcinia cambogia*” and “propionyl” has been corrected to “propionyl”. Applicants submit that these corrections would be evident to those with skill in the art, and specific support for these changes is found on pages 7-12 of the specification. The third entry in Table I, which describes food consumption in rats treated with L-carnitine, has been changed from “181.1” to “18.1” in order to correct a typographical error inserting the extra numeral “1” into this value. Support for the lower value is found in the description of the food consumption results at pages 8-9 of the specification, which indicates that “no changes compared to controls were noted . . . in rats treated with L-carnitine”.

While Claims 11-30 do not narrow the subject matter claimed in original Claims 1-10, they generally track and find support therein. Page 3 describes the various salts of L-carnitine or alkanoyl L-carnitine recited in Claim 15. The bottom of page 14 of the specification describes compositions comprising chromium as recited by Claim 22. Support for the methods of Claims 25-30 is found throughout the specification, and specifically in Tables 1-5 on pages 16-20 of the specification and in original Claim 10. Accordingly, the

Applicants do not believe that any new matter has been introduced. Applicants respectfully submit that Claims 11-30 are now ready for early examination on the merits.

Respectfully submitted,

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